CANINE BABESIOSIS IN THE DEVELOPED WORLD

START

VECTOR BORNE DISEASE

MSD Animal Health

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Peter Irwin graduated from the Royal Veterinary College, London University, in 1982 and after practising in the UK for a few years, moved to Australia where he earned a PhD working with canine babesiosis at James Cook University, Townsville, North Queensland. Peter completed a residency in small animal medicine at the University of Melbourne and is a registered specialist in canine internal medicine. Since 1998, Peter has been teaching small animal medicine and conducting research into vector-borne diseases at Murdoch University, Perth, Western Australia, and served as Principal (Dean) of the veterinary school 2014-2018. His current research focuses on tick-associated illness in humans and other animals in Australia.

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WHERE IS THE DISEASE MOST LIKELY TO BE FOUND?

Babesiosis occurs in domesticated dogs and wild canids on every continent on earth, with the exception of Antarctica. It is generally considered the most common and widespread of all the canine vector-borne diseases. Canine babesiosis is also called piroplasmosis, when species of *Theileria* parasites are included.

Geography, climate and socioeconomic factors play pivotal roles in delineating the distribution and clinical picture of babesiosis in dogs.

Local transmission of *Babesia* parasites requires a susceptible mammalian host population and a competent tick vector. Clinical disease risk is greatly increased where high densities of dogs are in close contact with all tick life-cycle stages, such as in **kennels, shelters and breeding establishments.**

WHERE IS THE DISEASE MOST LIKELY TO BE FOUND?

Ticks have evolved within distinct **climatic regions,** influenced predominately by the effects of temperature and relative humidity, underpinning the geographic distribution of the various *Babesia* species they transmit.

Studies investigating canine babesiosis epidemiology report a **seasonality** to babesiosis in dogs, coinciding with periods of tick activity and greater likelihood of exposure to infected ticks.

Reports in recent years have described the **emergence of canine babesiosis** around the world. Possible explanations for the apparent spread of canine babesiosis include: expansion in the ranges of vector ticks as a result of their spread by travelling dogs returning from endemic areas; climate change; increased veterinarian awareness of exotic disease; and, improved availability and sensitivity of diagnostic tests.

HOW DOES A DOG **BECOME INFECTED?**

An introduction to the causative agent

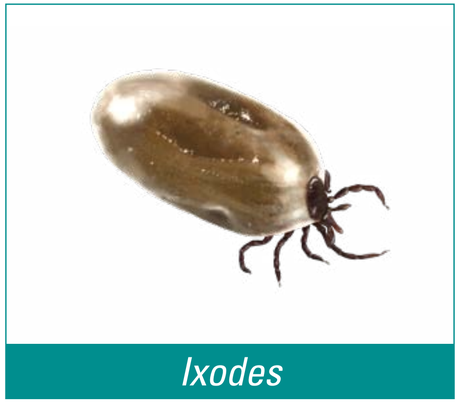
Canine babesiosis is a tick-borne, hemotropic disease with the majority of dogs becoming infected as a consequence a tick bite, however dog-to-dog transmission (i.e. bypassing the tick) occurs when the blood of one individual is mixed directly with that of another, as can occur through blood exchanged **during fighting,** via blood transfusions and transplacentally during gestation in an infected dam.

There are currently eleven **piroplasm species** recorded in dogs. *Babesia canis, B. rossi, B. vogeli, B. vulpes, B. conradae* and *B. gibsoni,* are the best recognised and most comprehensively studied forms of canine babesiosis, however, be aware that other species may arise unexpectedly in your area, or present in dogs with travel history.

Piroplasm species in dogs together with their tick vectors and reservoir hosts

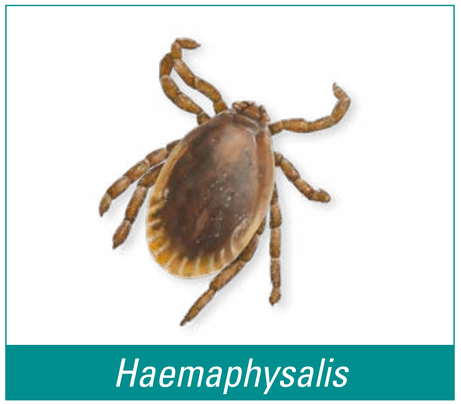
Vector

Canine babesiosis is vectored by hard ticks (Ixodidae) of the genera *Ixodes, Rhipicephalus, Haemaphysalis* and *Dermacentor,* although for some newly described species the vector, life cycle and reservoir hosts are unknown, and in the case of *B. negevi* the vector is suspected to be a soft tick.



Ixodes

Rhipicephalus



Haemaphysalis

Dermacentor

Proportion of vectors infected

The prevalence of infected ticks varies considerably between locations and tick species, as well as the method of collection. In general, the prevalence of piroplasm DNA is lower in unfed (questing) ticks collected in the environment compared with ticks that were removed from dogs:

- In a survey conducted in Russia, 20.3% of *D. reticulatus* ticks (n = 404) removed from dogs contained *Babesia canis* DNA.
- Yet just 1.5% of ticks removed from dogs in the UK were positive for babesial DNA, and only 10% of these were of a species known to cause disease in dogs *(B. vulpes).*
- In Malaysia 1.4% of *R. sanguineus* removed from dogs contained both *B. vogeli* or *B. gibsoni* DNA.

Babesia spp. are transovarially transmitted.

Reservoirs

The mammalian reservoir for *Babesia vogeli, B. canis* and *B. gibsoni* is the domestic dog, and these three parasites appear to have evolved and fully adapted to canine companion animals, however transmission of these piroplasms to wild canids may occur from time to time (e.g. *B. vogeli* to dingoes in Australia).

For other ***Babesia* (and *Theileria*) species** the reverse is true – wild animals maintain the parasite within sylvatic life cycles, and 'spill-over' (i.e. accidental infection) occurs from time to time, presumably when domestic dogs encounter the native tick vector. This situation is analogous to the way that people become infected with zoonotic tick-borne infections.

Probability of transmission

Probability of vector-borne transmission increases with:

- **High densities of dogs and ticks in the same environment**
- **Activities that facilitate the exchange of blood between dogs**

Transmission mechanics

Tick bite is the common way that dogs become infected and transmission dynamics align with tick life cycles. For the most part, canine babesiosis vectors are 'three-host' ticks, meaning that each life cycle stage (larvae, nymphs and adults) feed on a different individual mammalian host, detaching and molting prior to their next feed.

Babesia parasites can be transmitted in blood from an infected dog, either through bite wounds or blood transfusions, or **transplacentally,** although the documented evidence for this varies between species.

HOW DOES A DOG **BECOME INFECTED?**

Life cycle of the global tick *Rhipicephalus sanguineus*

7 Adults attach to the third host for feeding and mating

Adult female

1 Adult females drop off host to lay eggs

Larvae

2 Eggs hatch into six-legged larvae

3 Larvae feed on first host

Nymph

4 Larvae molt into nymphs after leaving first host

5 Nymphs feed on second host

Adult male

Adult female

6 Nymphs molt into adults after leaving second host

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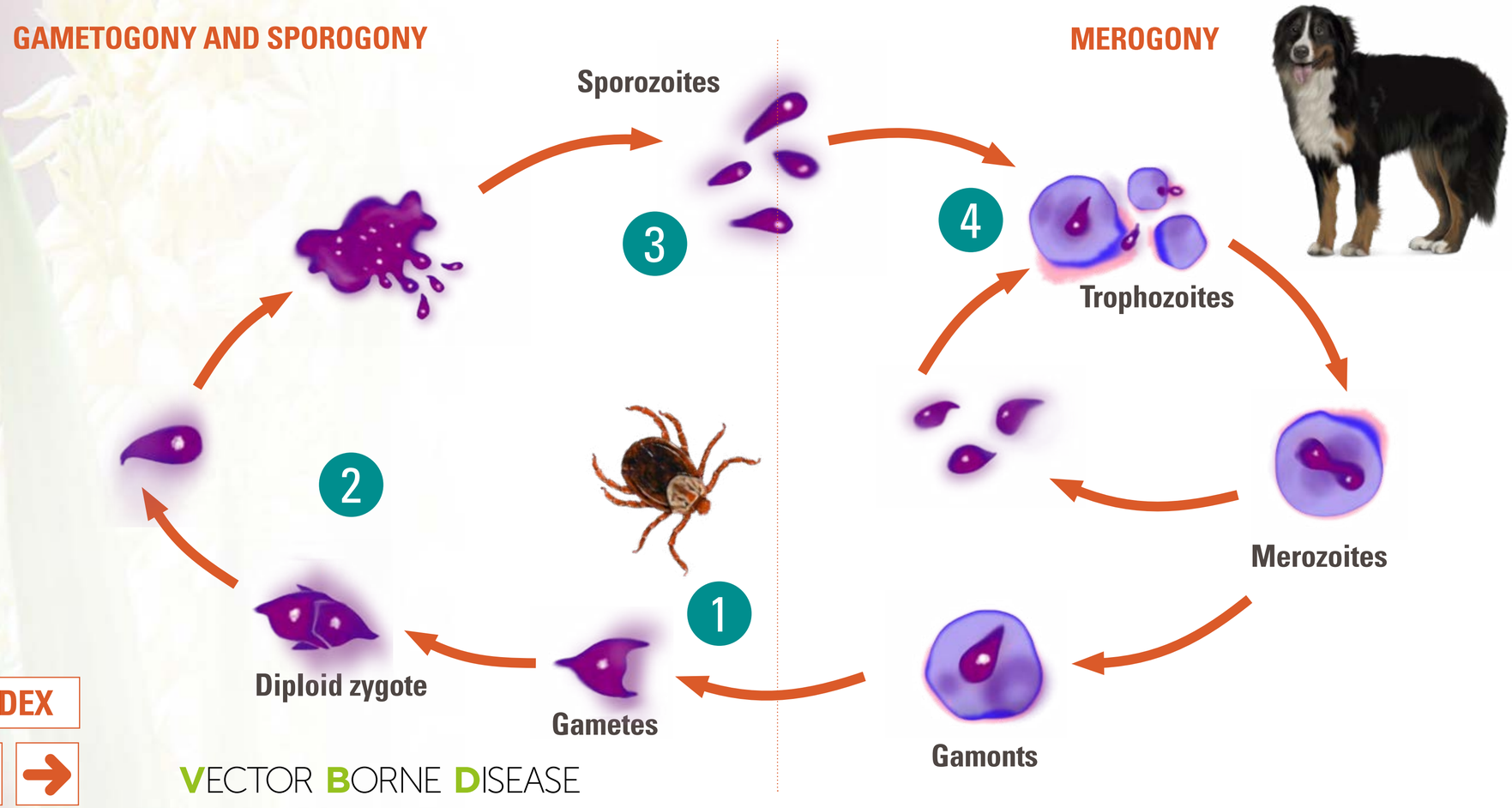
Life cycle of *Babesia* canis in the tick and dog



Click on for more information

WHAT BEHAVIORS
PUT A DOG AT RISK FOR THE DISEASE?

Activities

Activities and environments which bring dogs into contact with ticks will provide opportunities for infection. Kennels, shelters and breeding establishments, and places where ectoparasite control is poor (e.g. in low socioeconomic locations) potentially increase tick burdens and the risk of infection.

Fighting also puts dogs at risk of contracting babesiosis, and there are occasional reports of non-fighting dogs becoming infected after being attacked by infected dogs.

CAN A DOG BE INFECTED AND **NOT SHOW SIGNS?**

Infection *vs* disease

Subclinical infections occur with canine babesiosis, so potential infection in a patient without obvious disease is an important consideration, especially in endemic regions, and one that should be foremost in the veterinarian's mind. This is especially relevant for blood donation programs and the updated 2015 ACVIM Consensus Statement about canine and feline blood donor screening for infectious disease includes *Babesia* spp. amongst organisms to test for.

- Risk of subclinical disease (frequency in the population)
- Risk to the population from subclinically diseased dogs
- Tests that reveal a subclinically infected dog

Click on + for more information

WHAT CLINICAL SIGNS
DOES A SICK DOG SHOW AND WHY?

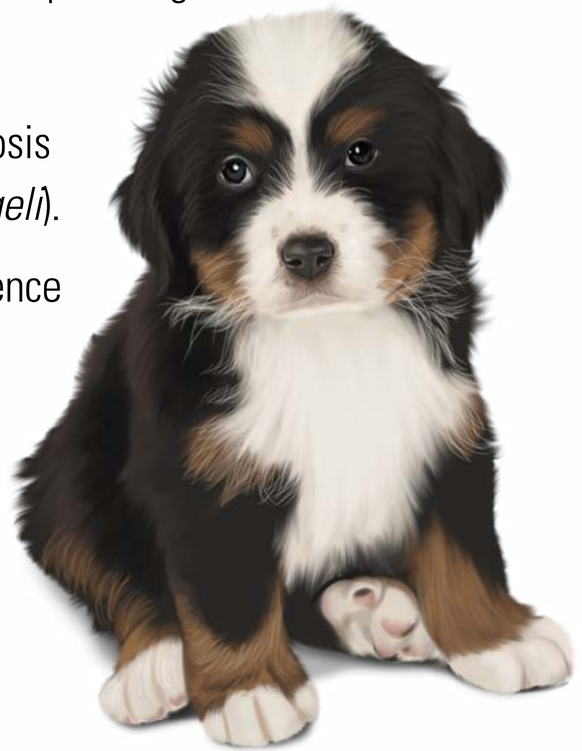
Pathogenesis

The severity of babesiosis ranges from subclinical infections to widespread organ failure and death.

Infected animals develop some level of **anemia** and some develop specific organ pathologies.

The pathogenicity of canine babesiosis depends on several factors:

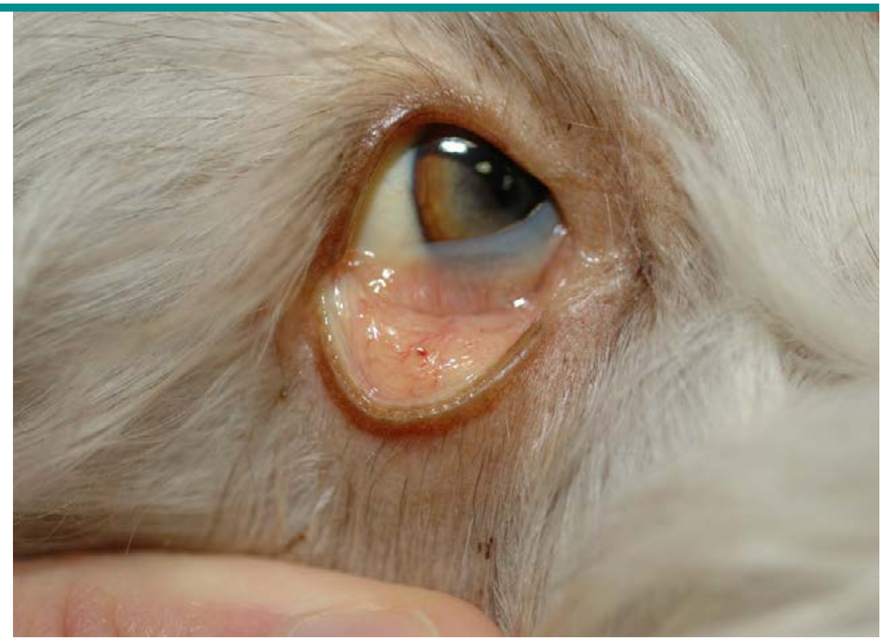
- It is primarily a function of the infecting species, with some forms of babesiosis *(B. canis and B. gibsoni)* considered more pathogenic than others (e.g. *B. vogeli*).
- Other factors such as **dog age and immune status,** the presence or absence of co-morbidities (e.g. immunosuppressive states), and presence of other tick-borne infections all contribute to the clinical outcome.



Early signs

Clinical signs of babesiosis are variable in the early (acute) stages of infection, however most dogs will develop lethargy, inappetence, weakness (progressing to collapse and death in some cases), and pallor (pale mucous membranes).

Pallor (pale mucous membranes) with icterus (jaundice) in the conjunctiva and sclera of a dog with acute hemolysis caused by babesiosis.



Progression

Depending on the virulence of the organism and its pathogenicity, progression of the clinical picture in dogs that survive the first few days may be mild (i.e. towards recovery) or associated with worsening signs:

- Epistaxis in some dogs
- Extreme pallor usually with jaundice (icterus) observed in areas of pale skin, in the mucous membranes, and in the sclera of the eyes
- Discolored urine (hemoglobinuria or bilirubinuria)

Hemoglobinuria (shown in a collecting bag); typical of dogs with severe intravascular hemolysis associated with acute babesiosis.

WHAT CLINICAL SIGNS DOES A SICK DOG SHOW AND WHY?

Prognostic factors

Severe babesiosis is characterized by a high mortality, but the prognosis is not necessarily correlated with clinical signs or parasitemia.

Clinicopathologic markers

Acute infections

Recovery indications

Uncomplicated babesiosis, that is dogs without severe metabolic derangements, tend to recover quickly (within 24-48 hours) once their hematocrit is restored to normal through blood transfusion and anti-babesial drug therapy.

Signs that indicate recovery include a **brighter demeanor, return of appetite, fever reduction (if present), and return of strength.**

WHAT DIAGNOSTIC TESTS SHOULD BE RUN
IN A DOG THAT IS SUSPECTED TO HAVE THE INFECTION/DISEASE?

Rapid, table-side

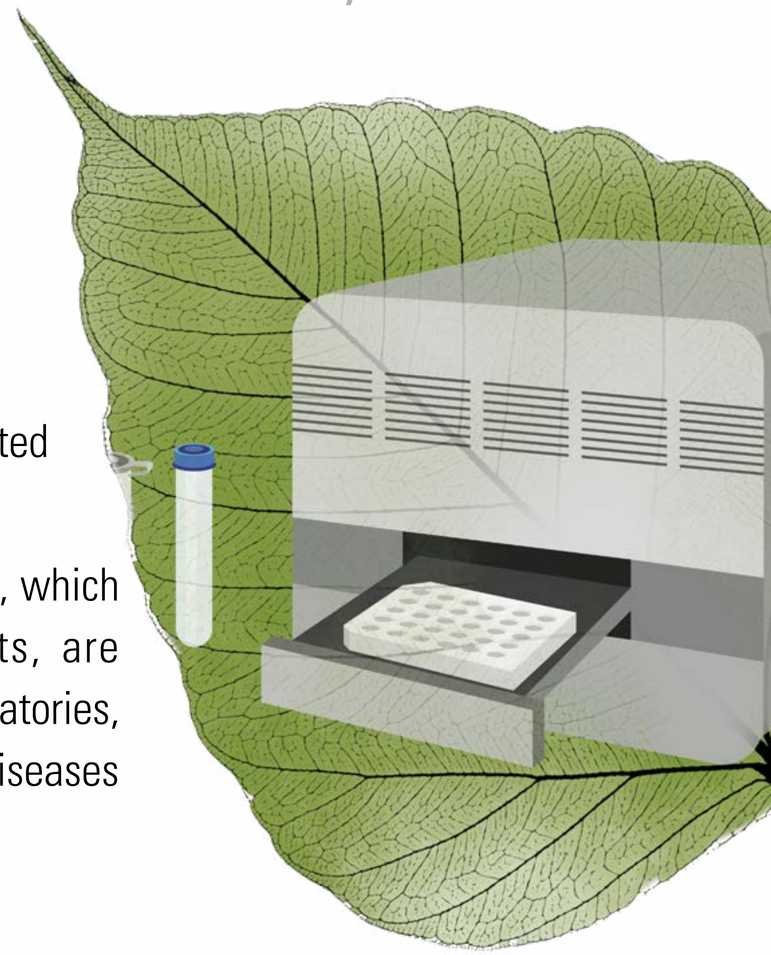
Highly sensitive and regionally-appropriate molecular (PCR-based) tests can be requested at local pathology laboratories and have significantly improved the diagnostic options available to practitioners.

A **thorough history** is essential. The physical examination should document the associated clinical signs

Diagnostic laboratories

Samples should be collected for **hematology, serum biochemistry** and **urinalysis** in all cases of suspected babesiosis.

Specific vector-borne disease panels, which include PCR and serological tests, are available from some commercial laboratories, and babesiosis is usually one of the diseases tested.



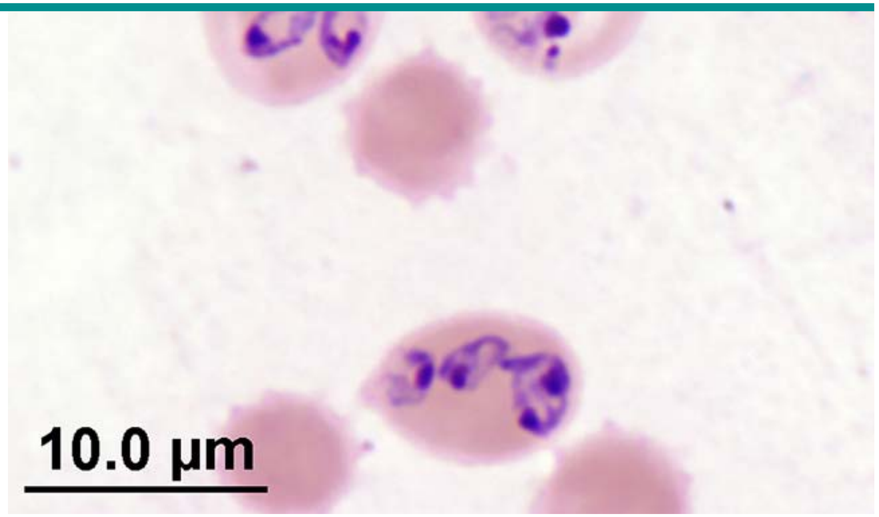
WHAT DIAGNOSTIC TESTS SHOULD BE RUN
IN A DOG THAT IS SUSPECTED TO HAVE THE INFECTION/DISEASE?

In hospital using microscope or similar equipment

Intra-erythrocytic inclusions can be seen in blood smears of dogs with **acute babesiosis.**

Microscopic evaluation of blood smears from dogs with chronic babesiosis is less likely to be successful given few parasites in the blood, however other important blood cell characteristics may be seen, and this diagnostic step should always be performed.

Variable morphology of large *Babesia* trophozoites *(Babesia vogeli).*

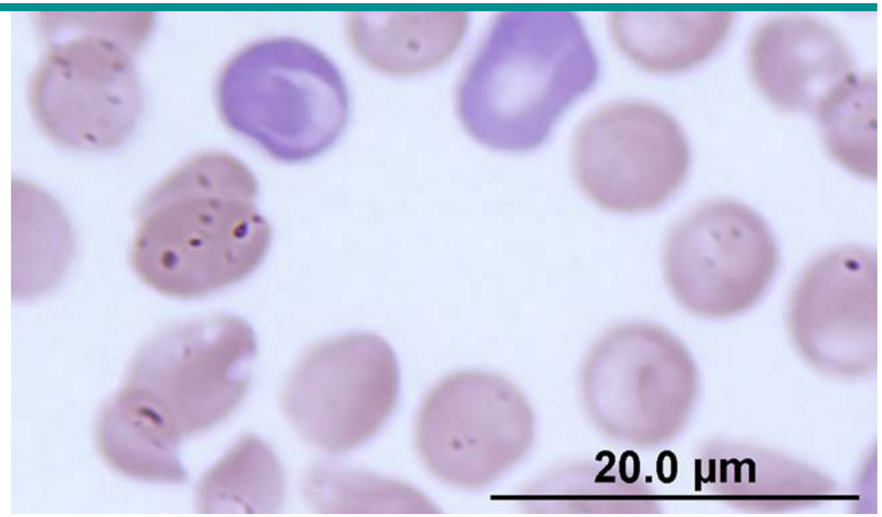


WHAT DIAGNOSTIC TESTS SHOULD BE RUN
IN A DOG THAT IS SUSPECTED TO HAVE THE INFECTION/DISEASE?

In hospital using microscope or similar equipment

A good blood smear with minimal artefact (e.g. stain precipitate, contamination) is critical.

This image shows a refractile artefact that could be mistaken for *Babesia* organisms. This most commonly occurs as a result of insufficient drying time of the blood smear prior to fixing and staining.



WHAT DIAGNOSTIC TESTS SHOULD BE RUN
IN A DOG THAT IS SUSPECTED TO HAVE THE INFECTION/DISEASE?

Test interpretation

Depending on the species of *Babesia* (and therefore the predominant pathophysiology), one or more organ systems may be affected during acute infection and this will be reflected in the laboratory results. Additionally, secondary injury associated with the inflammatory response, hypoxemia and shock may result in numerous metabolic derangements.

The hemogram usually includes hemolytic **anemia, thrombocytopenia and inflammatory leukogram** in cases of acute babesiosis.

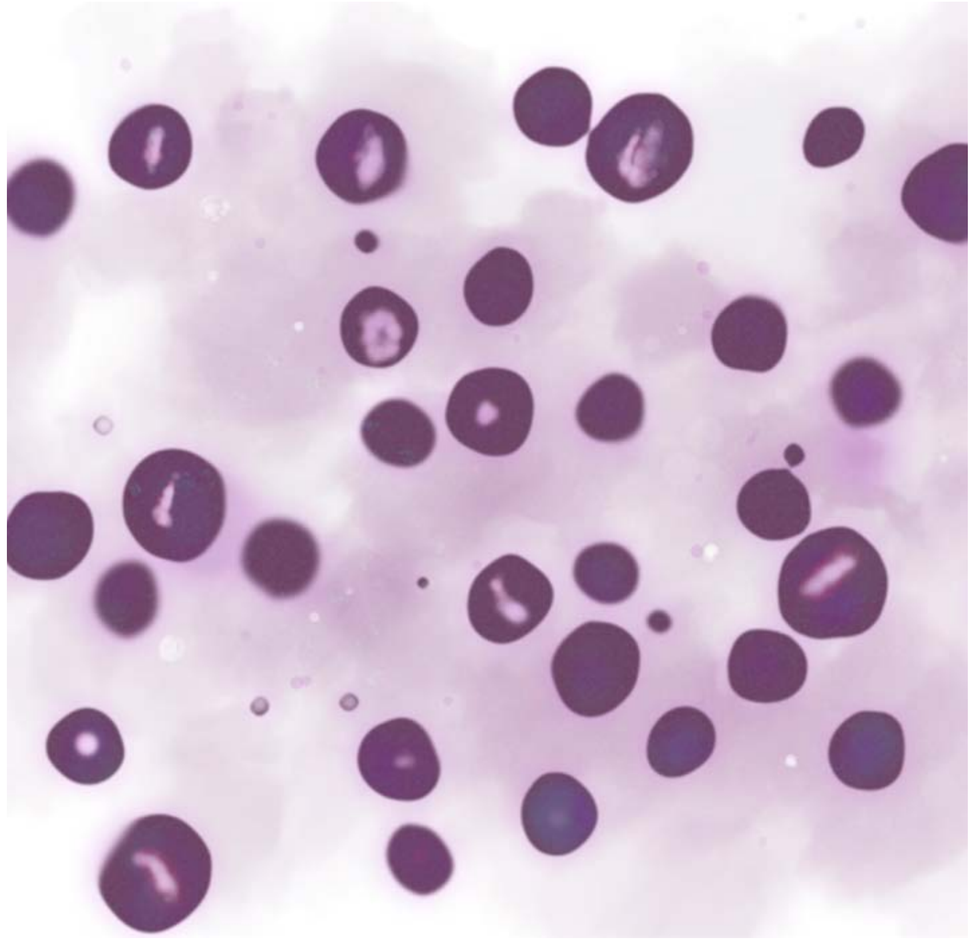
Plasma total solids/protein measurements are variable; hypoalbuminemia is reported with *B. canis, B. gibsoni* and *B. vulpes,* and a polyclonal gammopathy has been recorded in some cases, associated with hyperglobulinemia.

Serum biochemistry abnormalities reflect respective organ pathologies and acid-base disturbances associated with acute infections.

WHAT DIAGNOSTIC TESTS SHOULD BE RUN
IN A DOG THAT IS SUSPECTED TO HAVE THE INFECTION/DISEASE?

Differential diagnoses

Differential diagnoses should include other causes of **acute hemolysis** and other causes of systemic inflammatory response syndrome (SIRS) such as acute septicemia.



WHAT DIAGNOSTIC TESTS SHOULD BE RUN
IN A DOG THAT IS SUSPECTED TO HAVE THE INFECTION/DISEASE?

Acute *vs* convalescent

Death in complicated cases of babesiosis generally occurs within 24-48 hours after admission, but most cases start to recover soon after the administration of a blood transfusion, supportive fluid therapy, and anti-babesial drugs.

A rapid improvement in hematocrit is observed in dogs starting to recover, and other analytes, except for bilirubin, also quickly return to reference intervals in survivors.

Some dogs remain icteric for a week or more, and this is reflected in elevated bilirubin and orange urine for several days.

WHAT GENERAL TREATMENT STRATEGY IS RECOMMENDED FOR SICK DOGS?

Classes of drugs to use

Acute canine babesiosis treatment requires specific management of the metabolic derangements, with blood transfusion(s) and specific **anti-babesial drugs.**

- Anti-babesial drugs encompass aromatic diamidines, naphthoquinones, artemisinin derivatives and antibiotic classes. There are dissimilar drug susceptibilities, and an important consideration for the appropriate treatment of canine babesiosis is early **identification of the *Babesia* species.**
- Despite the worldwide importance of this disease there are relatively few robust studies on anti-babesial drug efficacy. Treatment protocols for canine babesiosis should not be expected to eliminate the pathogen.
- Combinations of tetracyclines (minocycline and doxycycline), metronidazole, clindamycin and enrofloxacin are used for atovaquone/azithromycin-resistant *B. gibsoni* infections, with variable efficacy. Without further data these combinations cannot be recommended.

WHAT GENERAL TREATMENT STRATEGY
IS RECOMMENDED FOR SICK DOGS?

Mono or combination therapy

The efficacy of mono-versus combination drug therapy for canine babesiosis needs further investigation.

Atovaquone/Buparvaquone + Azithromycin	The best-recognized therapeutic combinations are atovaquone or buparvaquone with the macrolide antibiotic azithromycin for the treatment of B. gibsoni and B. vulpes, respectively.
Diminazine aceturate + Imidocarb dipropionate/ Clindamycin/Metronidazole	Other combinations such as diminazine aceturate with imidocarb dipropionate, with clindamycin and/or metronidazole have shown efficacy in a few cases in uncontrolled studies.

WHAT GENERAL TREATMENT STRATEGY
IS RECOMMENDED FOR SICK DOGS?

Management of co-infections

Co-infections such as monocytic ehrlichiosis and anaplasmosis (*A. platys*) are common, especially with *B. vogeli* and should be treated with doxycycline (10 mg/kg q24h PO x 28 days).

WHAT GENERAL TREATMENT STRATEGY IS RECOMMENDED FOR SICK DOGS?

Supportive treatment strategies

Supportive treatment restores adequate tissue oxygenation by correcting anemia, dehydration and electrolyte disturbances, if present.

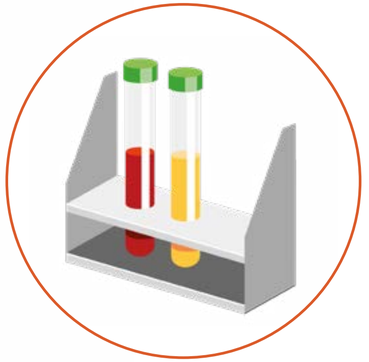
- Blood transfusions
- Fluid therapy
- Oxygen therapy
- Good nursing support
- Treating tick infestations

Click on + for more information

WHAT GENERAL TREATMENT STRATEGY IS RECOMMENDED FOR SICK DOGS?

Monitoring for response to treatment

Hematocrit, blood gases, electrolytes and renal function should be assessed at least daily during acute infection.



ARE OTHER PETS OR PEOPLE IN THE HOUSE AT RISK?

The risks to people from an infected/sick dog

Babesiosis is not contagious, in the sense that it is not readily transmitted between dogs although parasites may be transmitted through bite wounds (blood exchange). The presence of an infected dog indicates there is a risk to other dogs in the household from tick bite transmission.

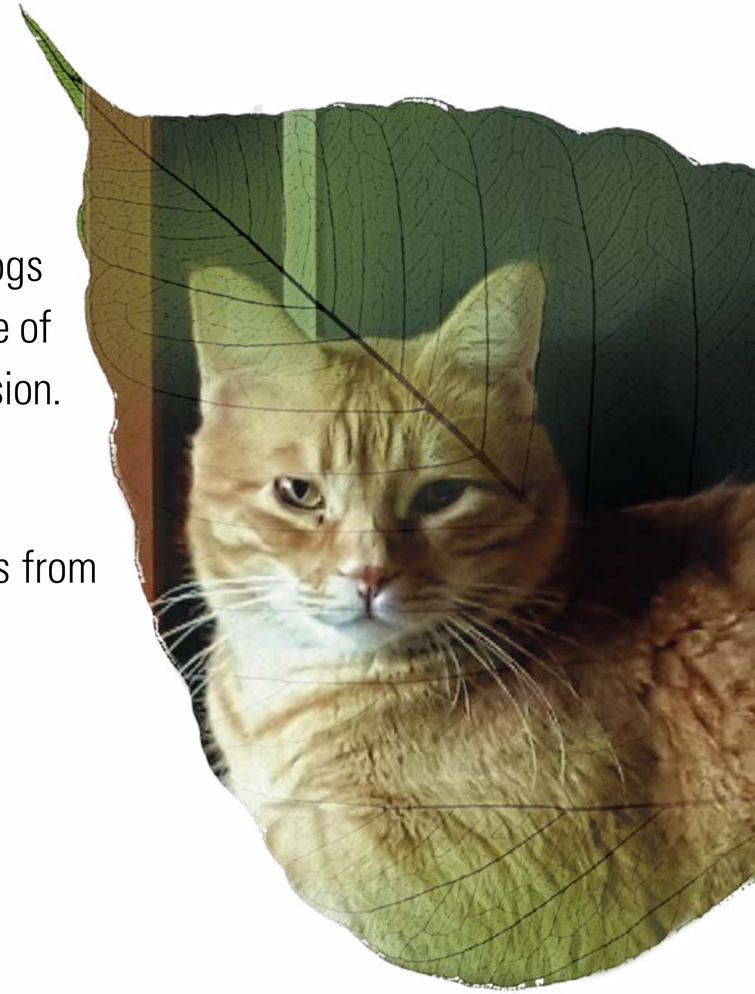
Other public health considerations

Canine babesiosis is not known to be zoonotic; although dog owners can face other risks from tick bites.

Can cats get this infection/disease?

No currently recognized agent of canine babesiosis infects cats.

- A *Babesia* parasite closely related to *B. canis* (sensu lato) may infect cats but is a distinct sub-species named *B. canis* subsp. *presentii.*



WHAT ARE SOME RECOMMENDATIONS AROUND PREVENTION STRATEGIES?

How to avoid the vector

There are recent remarkable advances in the types and range of acaricidal drugs available, with **new compounds** replacing earlier generations of drugs that were potentially more toxic to the mammalian host.

Increasing owner compliance with treatment recommendations is an important goal in acaricide treatment.

Is routine testing recommended?

Blood donors

Routine testing for the safety and suitability of dogs to act as blood donors is recommended.

Other animals

Routine testing of other apparently healthy dogs is of no value and chronically infected dogs are difficult to detect, even using PCR. Treatment is not generally curative, therefore routine testing may not offer much value.

WHAT ARE SOME RECOMMENDATIONS AROUND PREVENTION STRATEGIES?

General thoughts on preventive treatments

Regular acaricidal and tick prophylactic treatment is recommended in endemic areas, together with avoidance of dog fighting and pre-screening of blood donors.

Ensuring owner compliance is a key goal for preventive treatment.

Is there a vaccine?

A vaccine for *B. canis* is available in Europe and appears to have reasonable **efficacy for preventing** infection with this form of babesiosis.

WHAT DOES THE FUTURE LOOK LIKE?

What are the changes being seen with the disease?

The geographic range of canine babesiosis appears to be expanding into new regions, including northward extension into cooler climates of Europe and North America.

Autochthonous B. canis cases are now present in the United Kingdom and veterinarians everywhere need to be ever-vigilant for the unexpected appearance of vector-borne diseases in day-to-day clinical practice.

Wide application of molecular diagnostic techniques makes it inevitable that new species will be discovered, and some could be significant pathogens. Countering this increasing disease burden of disease is the availability of novel and highly effective acaricidal drugs.

FURTHER READING

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